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EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/763,992	COHEN ET AL.	
	Examiner	Art Unit	
	Laura B. Goddard, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed After Final July 21, 2006 in response to the Office Action of April 19, 2006, is acknowledged and has been entered. Upon review and reconsideration, the finality of the previous Office Action has been withdrawn.

Previously pending claim 1 has been amended. Claims 1-9 are currently being examined.

Claim Objections

2. Claims 1-9 are objected to for containing subject material that is drawn to a non-elected invention. The claims recite a method for detecting the presence of a target prostate cancer associated (PS112) polynucleotide or mRNA in a test sample. Applicants elected the invention of detecting SEQ ID NO:9. The claims as currently constituted encompass non-elected PS112 polynucleotides, SEQ ID NOs:1-8 and 10 (see Election/Restriciton in the Office Action mailed July 21, 2005). Appropriate correction is required. The objection may be obviated by amending the claims to read on a method of detecting the presence of the target cancer associated (PS112) polynucleotide SEQ ID NO:9.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: hybridization of the PS112-specific polynucleotide or oligonucleotide to the targeted PS112 polynucleotide for detection and isolation of or labeling of the hybridized polynucleotide for detection. As currently constituted, claim 1 recites only the steps of contacting said test sample with at least one PS112-specific polynucleotide or complement thereof and detecting the presence of said target PS112 polynucleotide. Hybridization of the PS112-specific polynucleotide to the targeted PS112 polynucleotide and detection of the hybridized pair must occur for detection of a PS112 polynucleotide.

4. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The use of laboratory designations only to identify a particular polynucleotide such as PS112 renders the claims indefinite because different laboratories may use the same laboratory designation to define completely distinct polynucleotides. Amendment of the claims, for example, to include the **SEQ ID number** which unambiguously defines a given polynucleotide, would obviate the rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for **a method of detecting the presence of the PS112 polynucleotide, SEQ ID NO:9, or corresponding mRNA, in a test sample comprising utilizing a PS112-specific polynucleotide or oligonucleotide and detecting the presence of said PS112 polynucleotide or mRNA in the test sample wherein said PS112-specific polynucleotide or oligonucleotide has 100% identity to SEQ ID NO:9, and wherein said PS112-specific polynucleotide or oligonucleotide has a length of at least 15 nucleotides**, does not reasonably provide enablement for a method of detecting the presence of a PS112 polynucleotide in a test sample comprising utilizing a PS112-specific polynucleotide, oligonucleotide, or complete complement thereof and detecting the presence of said PS112 polynucleotide in the test sample, wherein said PS112-specific polynucleotide or oligonucleotide has at least 80% identity to a polynucleotide selected from the group consisting of SEQ ID NO:9 and complements thereof, said complements having a length and a sequence of at least 15 nucleotides and a method of detecting PS112 mRNA comprising utilizing said PS112-specific polynucleotides or oligonucleotides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to

practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to:

a method of detecting the presence of PS112 polynucleotide in a test sample comprising (a) contacting said test sample with at least **one PS112-specific polynucleotide or complete complement thereof**; (b) and detecting the presence of said PS112 polynucleotide in the test sample wherein said PS112-specific polynucleotide has **at least 80%** identity to a polynucleotide selected from the group consisting of SEQ ID NO:9 **and complements thereof**, said complements having a length and a sequence of at least 15 nucleotides (claims 1 and 2);

a method for detecting PS112 mRNA in a test sample comprising (a) performing reverse transcription with at least one primer to produce cDNA; (b) amplifying the cDNA from step (a) using PS112 oligonucleotides as sense primers to obtain PS112 amplicon;

and (c) detecting the presence of said PS112 amplicon in the test sample wherein the PS112 oligonucleotides utilized in steps (a) and (b) have **at least 80% identity** to a sequence selected from the group consisting of SEQ ID NO:9 and **complements thereof**, said complements having a length and a sequence of at least 15 nucleotides (claims 3-5); and

a method of detecting a PS112 polynucleotide in a test sample comprising (a) contacting said test sample with at least one PS112 oligonucleotide as a sense primer and with at least one PS112 oligonucleotide as an anti-sense primer and amplifying to obtain a first stage reaction product; (b) contacting said first stage reaction product with at least one other PS112 oligonucleotide to obtain a second reaction product, with the proviso that the other PS112 oligonucleotide is located 3' to the PS112 oligonucleotide utilized in step (a) and is **complementary** to said first stage reaction product; and (c) detecting said second stage reaction product as an indication of the presence of PS112 polynucleotide, wherein the PS112 oligonucleotides utilized in steps (a) and (b) have at least **80% identity** to a sequence selected form the group consisting of SEQ ID NO:9 and **complements thereof**, said complements having a length and a sequence of at least 15 nucleotides (claims 6-9).

The claims are broadly drawn to a method of detecting the presence of **any PS112 polynucleotide or mRNA**, wherein the methods comprise utilizing **any PS112-specific polynucleotides or oligonucleotides** that have at least 80% identity to SEQ ID NO:9 or identity to complements of SEQ ID NO:9, wherein the complements the PS112-specific polynucleotides or oligonucleotides have identity to are at least 15

nucleotides in length. Claims 1 and 2 are broadly drawn to a method of detecting the presence of PS112 polynucleotide, wherein the methods comprise utilizing **any complement to a PS112-specific polynucleotides or oligonucleotides** that is not required to be fully complementary to a PS112-specific polynucleotides or oligonucleotides and could be of **any length**. It is noted that there is also **no required length for the PS112-specific polynucleotides or oligonucleotides** used to detect PS112, nor are they required to have 100% identity to the targeted PS112 polynucleotide. It is noted that the complements of SEQ ID NO:9 are not required to be **complete complements**, hence the claims are drawn to a broad range of complements to which the PS112-specific polynucleotides or oligonucleotides presumably hybridize to for detection.

The specification discloses SEQ ID NO:9 as a PS112 polynucleotide, wherein a high level of mRNA for SEQ ID NO:9 was detected in malignant prostate tissue but not in normal prostate tissue (p. 58; Table 1). The mRNA was detected by isolation from the tissue sample, hybridization with a radioactively labeled probe, and visualized by gel electrophoresis and autoradiography (Example 4; p. 57-58). The specification further discloses In Situ Hybridization using detectable nucleic acid hybridization probes (Example 7) and RT-PCR (Example 8) for the detection of a PS112 polynucleotide or mRNA. It is unclear exactly what primers or probes were used to detect PS112 in the Examples.

One cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide guidance or examples for detecting

PS112 polynucleotide comprising contacting a test sample with any length of PS112-specific polynucleotide or oligonucleotide or any complement thereof, any PS112-specific polynucleotide that has less than 100% identity to PS112, or any PS112-specific polynucleotide that has any length and is not 100% complementary to SEQ ID NO:9. Those of skill in the art recognize that specific detection of a polynucleotide requires probes or primers that have 100% identity to the targeted polynucleotide so that only the targeted polynucleotide is detected and/or amplified. A complement is not always a 100% match of sequence. Further, those of skill in the art recognize that specific detection of a polynucleotide requires a primer or probe of at least nucleotides in length for specificity in sequence to a targeted polynucleotide. Otherwise, the specificity of detection is decreased and the polynucleotide detected may not be the targeted PS112 polynucleotide. Simmler et al (HiCOMB 2006, Fifth IEEE International Workshop on High Performance Computational Biology, "Real-Time Primer Design for DNA Chips") teach the complex requirements for primers to specifically anneal to the targeted DNA, including factors that affect hybridization conditions such as primer length, melting temperature, self-annealing, GC content, and secondary structure (p. 1-4; Section 3.1). Simmler et al teach optimal primer selection and the variables considered for selecting primers (p. 4-5, Section 3.2). Given the teaching of Simmler et al and what is conventionally known in the art for the specific detection of a target polynucleotide, one of skill in the art could not predictably detect PS112 polynucleotide or mRNA comprising utilizing any PS112-specific polynucleotide, oligonucleotide, or complement thereof of any length, or of less than 100% identity to SEQ ID NO:9. While

Applicant may argue that some of the claimed PS112-specific polynucleotides, oligonucleotides or complements thereof may hybridize to and/or amplify and detect PS112, those of skill in the art recognize that shorter primers or probes and/or of lower identity to the targeted polynucleotide have lower specificity, meaning they will detect polynucleotides that are not PS112, hence do not enable the claimed method

Therefore, in view of the quantity of experimentation necessary to detect PS112 using the broadly claimed PS112-specific polynucleotides or oligonucleotides or complements thereof, the state of the art, the breadth of the claims, lack of guidance in the specification, and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as broadly claimed.

6. Claims 3-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for **a method of detecting a target prostate cancer associated (PS112) mRNA in a test sample comprising contacting said test sample with a forward and reverse primer pair to produce cDNA**, does not reasonably provide enablement for a method of detecting a target prostate cancer associated (PS112) mRNA in a test sample comprising contacting said test sample with at least one primer in order to produce cDNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a method for detecting PS112 mRNA in a test sample comprising (a) performing reverse transcription with **at least one primer to produce cDNA**; (b) amplifying the cDNA from step (a) using PS112 oligonucleotides as sense primers to obtain PS112 amplicon; and (c) detecting the presence of said PS112 amplicon in the test sample wherein the PS112 oligonucleotides utilized in steps (a) and (b) have at least 80% identity to a sequence selected from the group consisting of SEQ ID NO:9 and complements thereof, said complements having a length and a sequence

of at least 15 nucleotides (claims 3-5). The claims are broadly drawn to a method of detecting PS112 mRNA comprising utilizing **one primer** for reverse transcription (RT) to produce cDNA.

Those of skill in the art recognize that two primers, a forward and reverse pair, are required for RT-PCR to produce cDNA. The Nucleic Acid Facility of The Huck Institutes of the Life Sciences at Penn State teach the requirement of two primers required for RT-PCR by stating: "Every sequence requires a set of forward and reverse primers" (p. 2, section III). Hence, one of skill in the art could not predictably produce cDNA from mRNA comprising performing RT with one primer.

Therefore, the state of the art, the breadth of the claims, lack of guidance in the specification, and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as broadly claimed.

7. All other rejections recited in the Office Action mailed April 19, 2006, are hereby withdrawn.

8. **Conclusion:** No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Laura B Goddard, Ph.D.
Examiner
Art Unit 1642

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER